

**Amendments to the Claims:**

This listing of claims will replace all prior versions and listings of claims in the application.

**Listing of Claims:**

1-28 (Cancelled)

29. (Currently Amended) A composition for treating or preventing arthritis or other degenerative disease, said composition comprising an anti-arthritis or anti-inflammatory one or more polypeptide fragment consisting essentially of at least a portion of the NC4 domain of collagen type IX-alpha 1 chain and a carrier having at least 65% amino acid identity to SEQ ID NO: 14, wherein said fragment induces tolerance to cartilage.

30. (Currently Amended) The composition of claim 29, wherein the polypeptide fragment has a molecular weight of:

- a) less than 30,000 Da, or
- b) less than 30,000 Da and greater than or equal to 10,000 Da.

31. (Currently Amended) The composition of claim 29, wherein the polypeptide fragment has an amino acid length of less than 250 amino acids.

32. (Currently Amended) The composition of claim 29, wherein the NC4 domain of collagen type IX-alpha 1 chain comprises an amino acid sequence having polypeptide fragment has identity to SEQ ID NO: 1, SEQ ID NO: 14, SEQ ID NO: 16, or SEQ ID NO: 18 that is:

- a) at least 8070%;
- b) at least 90%; or
- c) 100%.

33. (Currently Amended) The composition of claim 29, wherein the composition comprises one or more polypeptide fragment selected from:

- (a) K/QSVS/V/A/EFSYKG [SEQ ID NO: 20];
- (b) KI/LMIG/SVER/TST [SEQ ID NO: 21];
- (c) KLGNNVDFRI [SEQ ID NO: 4];
- (d) R/KI/VES/TLP/NIKPR/KG [SEQ ID NO: 22];
- (e) KH/N/YWS/N/TIWQIQDS/AGK/R [SEQ ID NO: 23];

- (f) RIGQDDLPGFDLISQFQI/VD/EKA [SEQ ID NO: 24];
- (g) R/S/N/AL/IYPN/SGLPE/DEYSFLTTFR [SEQ ID NO: 25];
- (h) FS/LN/HLP/SS/FLFDSQ/RWHK1/L [SEQ ID NO: 26]; and
- (i) R/TS/TSA/VTLFV/IDCN/IR/KI/V [SEQ ID NO: 27].

- (i) — residues Ile21—Gly182 of SEQ ID NO: 1;
- (ii) — residues Lys60—Arg181 of SEQ ID NO: 1;
- (iii) — residues Arg72—Arg181 of SEQ ID NO: 1;
- (iv) — residues Lys98—Gly182 of SEQ ID NO: 1;
- (v) — residues Lys123—Gly182 of SEQ ID NO: 1;
- (vi) — residues Ile24—Val208 of SEQ ID NO: 14;
- (vii) — residues Asp29—Val208 of SEQ ID NO: 14;
- (viii) — residues Asp29—Met215 of SEQ ID NO: 14;
- (ix) — residues Asp29—Pro209 of SEQ ID NO: 14;
- (x) — residues Asp29—Arg245 of SEQ ID NO: 14;
- (xi) — residues Asp29—Met96 of SEQ ID NO: 14, or
- (xii) — residues Trp108—Val208 of SEQ ID NO: 14.

34. (Currently Amended) The composition of claim 29, wherein the composition comprises one or more polypeptide fragment selected from: at least one of SEQ ID NOS: 2-11:

- (a) K/QSVS/VFSYKG [SEQ ID NO: 28];
- (b) KIMIGVERTS [SEQ ID NO: 3, 10];
- (c) RIESLPIKPRG [SEQ ID NO: 5];
- (d) KH/NWS/NIWQIQDSGK [SEQ ID NO: 29];
- (e) RIGQDDLPGFDLISQFQI/VDKA [SEQ ID NO: 30];
- (f) RH/NLYPN/SGLPEEYSFLTTFR [SEQ ID NO: 31];
- (g) FSNLP/SSLFDSQWCHK1 [SEQ ID NO: 32]; and
- (h) RSSATLFVDCNRI [SEQ ID NO: 11].

35. (Currently Amended) A method of inducing tolerance to at least one antigenic component of cartilage in an individual, the method comprising administering to the individual the composition of claim 29, wherein said administering induces said tolerance.

36. (Currently Amended) The method of claim 35, wherein the administered composition comprises one or more polypeptide fragment having has a molecular weight of:

- a) less than 30,000 Da, or
- b) less than 30,000 Da and greater than or equal to 10,000 Da.

37. (Currently Amended) The method of claim 35, wherein the administered composition comprises one or more polypeptide fragment having has an amino acid length of less than 250 amino acids.

38. (Currently Amended) The method of claim 35, wherein the ~~NC4 domain of collagen type IX alpha 1 chain comprises an amino acid sequence having administered composition comprises one or more polypeptide fragment having identity to SEQ ID NO: 1, SEQ ID NO: 14, SEQ ID NO: 16, or SEQ ID NO: 18~~ that is:

- a) at least 8070%;
- b) at least 90%; or
- c) 100%.

39. (Currently Amended) The method of claim 35, wherein the composition comprises one or more polypeptide comprises fragment selected from:

- (a) K/QSVS/V/A/EFSYKG [SEQ ID NO: 20];
  - (b) KI/LMIG/SVER/TS/T [SEQ ID NO: 21];
  - (c) KLGNNVDFRI [SEQ ID NO: 4];
  - (d) R/KI/VES/TLP/NIKPR/KG [SEQ ID NO: 22];
  - (e) KH/N/YWS/N/TIWOIQDS/AGK/R [SEQ ID NO: 23];
  - (f) RIGQDDLPGFDLISQFQI/VD/EKA [SEQ ID NO: 24];
  - (g) R/SH/N/AL/IYPN/SGLPE/DEYSFLTTFR [SEQ ID NO: 25];
  - (h) FS/LN/HLP/SS/FLFDSQ/R/WHKI/L [SEQ ID NO: 26]; and
  - (i) R/TS/TSA/VTLFV/IDCN/IR/KI/V [SEQ ID NO: 27].
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- (i) — residues Ile21—Gly182 of SEQ ID NO: 1;
  - (ii) — residues Lys60—Arg181 of SEQ ID NO: 1;
  - (iii) — residues Arg72—Arg181 of SEQ ID NO: 1;
  - (iv) — residues Lys98—Gly182 of SEQ ID NO: 1;
  - (v) — residues Lys123—Gly182 of SEQ ID NO: 1;
  - (vi) — residues Ile24—Val208 of SEQ ID NO: 14;
  - (vii) — residues Asp29—Val208 of SEQ ID NO: 14;
  - (viii) — residues Asp29—Met215 of SEQ ID NO: 14;
  - (ix) — residues Asp29—Pro209 of SEQ ID NO: 14;
  - (x) — residues Asp29—Arg245 of SEQ ID NO: 14,

- (xi) — residues Asp29 — Met96 of SEQ ID NO: 14, or
- (xii) — residues Trp108 — Val208 of SEQ ID NO: 14.

40. (Currently Amended) The method of claim 35, wherein the composition comprises one or more polypeptidc ecomprises fragment selected from: at least one of SEQ ID NOS: 2-11.

- (a) K/QSVS/VFSYKG [SEQ ID NO: 28];
- (b) KIMIGVERTS [SEQ ID NO: 3, 10];
- (c) RIESLPIKPRG [SEQ ID NO: 5];
- (d) KH/NWS/NIWQIQDSGK [SEQ ID NO: 29];
- (e) RIGQDDLPGFDLISQFQI/VDKA [SEQ ID NO: 30];
- (f) RH/NLYPN/SGLPEEYSFLTTFR [SEQ ID NO: 31];
- (g) FSNLP/SSLFDSQWHKI [SEQ ID NO: 32];
- (h) RSSATLFVDCNRI [SEQ ID NO: 11].

41. (Previously Presented) The method of claim 35, wherein the individual is a naive individual.

42. (Currently Amended) The method of claim 35, A method for treating or preventing wherein said administering treats or prevents a degenerative condition or disease in an individual comprising administering to the individual the composition of claim 29.

43. (Previously Presented) The method of claim 42, wherein the degenerative condition or disease is arthritis or a musculoskeletal degenerative condition.

44. (Previously Presented) The method of claim 43, wherein the degenerative condition or disease is rheumatoid arthritis, osteoarthritis, disc degeneration, or osteoporosis.

45. (Currently Amended) The method of claim 42, wherein the administered composition comprises one or more polypeptide fragment having has a molecular weight of:

- a) less than 30,000 Da, or
- b) less than 30,000 Da and greater than or equal to 10,000 Da.

46. (Currently Amended) The method of claim 42, wherein the administered composition comprises one or more polypeptide fragment having has an amino acid length of less than 250 amino acids.

47. (Currently Amended) The method of claim 42, wherein the NC4 domain of collagen type IX alpha 1 chain comprises an amino acid sequence administered composition comprises one or more polypeptide fragment having identity to SEQ ID NO: 1, SEQ ID NO: 14, SEQ ID NO: 16, or SEQ ID NO: 18 that is:

- a) at least 80%;
- b) at least 90%; or
- c) 100%.

48. (Currently Amended) The method of claim 42, wherein the composition comprises one or more polypeptide comprises fragment selected from:

- (a) K/QSVS/V/A/EFSYKG [SEQ ID NO: 20];
  - (b) KI/LMIG/SVER/TS/T [SEQ ID NO: 21];
  - (c) KLGNNVDFR1 [SEQ ID NO: 4];
  - (d) R/KI/VES/TLP/NIKP/R/KG [SEQ ID NO: 22];
  - (e) KH/N/YWS/N/TIWQIQDS/AGK/R [SEQ ID NO: 23];
  - (f) RIGQDDLPGFDLISQFQJ/VD/EKA [SEQ ID NO: 24];
  - (g) R/SH/N/AL/IYPN/SGLPE/DEYSFLTTFR [SEQ ID NO: 25];
  - (h) FS/LN/HLP/SS/FLFDSQ/RWHKI/L [SEQ ID NO: 26]; and
  - (i) R/TS/TSA/VTLFV/IDCN/IR/KI/V [SEQ ID NO: 27].
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- (i) residues Ile21-Gly182 of SEQ ID NO: 1;
  - (ii) residues Lys60-Arg181 of SEQ ID NO: 1;
  - (iii) residues Arg72-Arg181 of SEQ ID NO: 1;
  - (iv) residues Lys98-Gly182 of SEQ ID NO: 1;
  - (v) residues Lys123-Gly182 of SEQ ID NO: 1;
  - (vi) residues Ile24-Val208 of SEQ ID NO: 14;
  - (vii) residues Asp29-Val208 of SEQ ID NO: 14;
  - (viii) residues Asp29-Met215 of SEQ ID NO: 14;
  - (ix) residues Asp29-Pro209 of SEQ ID NO: 14;
  - (x) residues Asp29-Arg245 of SEQ ID NO: 14;
  - (xi) residues Asp29-Met96 of SEQ ID NO: 14, or
  - (xii) residues Trp108-Val208 of SEQ ID NO: 14.

49. (Currently Amended) The method of claim 42, wherein the composition comprises one or more polypeptide comprises fragment selected from: at least one of SEQ ID NOs: 2-11.

- (a) K/QSVS/VFSYKG [SEQ ID NO: 28];
- (b) KIMIGVERTS [SEQ ID NO: 3, 10];
- (c) RIESLPIKPRG [SEQ ID NO: 5];
- (d) KH/NWS/NIWQIQDSGK [SEQ ID NO: 29];
- (e) RIGQDDLPGLFDLISQFQI/VDKA [SEQ ID NO: 30];
- (f) RH/NLYPN/SGLPEEYSFLTTFR [SEQ ID NO: 31];
- (g) FSNLP/SSLFDSQWHKI [SEQ ID NO: 32]; and
- (h) RSSATLFVDCNRI [SEQ ID NO: 11].

50. (Previously Presented) The method of claim 42, wherein the individual is a naive individual.

51. (Currently Amended) A method for isolating a polypeptide fragment having anti-arthritis or anti-inflammatory activity comprising:

- (i) incubating a connective tissue in a buffered autolysis medium to release a mixture of polypeptide fragments containing GAG polypeptide fragments and non-GAG polypeptide fragments;
- (ii) fractionating the polypeptide fragments by size to produce a fraction of protein polypeptides fragments having a molecular weight of less than 30 KDa;
- (iii) separating GAG-polypeptide fragments from non-GAG polypeptide fragments; and
- (iv) recovering one or more non-GAG polypeptides fragment having a molecular weight less than 30 KDa, and having anti-arthritis or anti-inflammatory activity.

52. (Previously Presented) The method of claim 51, wherein the autolysis medium has a pH range of:

- a) about pH 2.5 to about pH 8.5;
- b) pH 3.5 to about pH 8;
- c) pH 4 to about pH 7; or
- d) pH 4.5 to about pH 7.

53. (Currently Amended) [[A]]The method of claim 35, wherein said administering for preventing treats or prevents an autoimmune response in an individual to at least one antigenic component of cartilage comprising administering the individual the composition of claim 29.

54. (Currently Amended) The method of claim 53, wherein the administered composition comprises one or more polypeptide fragment having has a molecular weight of:

- a) less than 30,000 Da, or
- b) less than 30,000 Da and greater than or equal to 10,000 Da.

55. (Currently Amended) The method of claim 53, wherein the polypeptide fragment has an amino acid length of less than 250 amino acids.

56. (Currently Amended) The method of claim 53, wherein the NC4 domain of collagen type IX alpha 1 chain comprises an amino acid sequence administered composition comprises one or more polypeptide fragment having identity to SEQ ID NO: 1, SEQ ID NO: 14 ,SEQ ID NO: 16, or SEQ ID NO: 18 that is:

- a) at least 80%;
- b) at least 90%; or
- c) 100%.

57. (Currently Amended) The method of claim 53, wherein the administered composition comprises one or more polypeptide comprises fragment selected from:

- (a) K/QSVS/V/A/EFSYKG [SEQ ID NO: 20];
- (b) KI/LMIG/SVER/TS/T [SEQ ID NO: 21];
- (c) KLGNVNDFRI [SEQ ID NO: 4];
- (d) R/KI/VES/TLP/NIKPR/KG [SEQ ID NO: 22];
- (e) KH/N/YWS/N/TIWQIQDS/AGK/R [SEQ ID NO: 23];
- (f) RIGQDDLPGFDLISQFQI/VD/EKA [SEQ ID NO: 24];
- (g) R/SH/N/AL/IYPN/SGLPE/DEYSFLTTFR [SEQ ID NO: 25]; and
- (h) FS/LN/HLP/SS/FLFDSQ/RWHKL [SEQ ID NO: 26].
- (i) R/TS/TSA/VTLFV/IDCN/IR/KI/V [SEQ ID NO: 27].

- (i) residues Ile21-Gly182 of SEQ ID NO: 1;
- (ii) residues Lys60-Arg181 of SEQ ID NO: 1;
- (iii) residues Arg72-Arg181 of SEQ ID NO: 1;
- (iv) residues Lys98-Gly182 of SEQ ID NO: 1;
- (v) residues Lys123-Gly182 of SEQ ID NO: 1;
- (vi) residues Ile24-Val208 of SEQ ID NO: 14;
- (vii) residues Asp29-Val208 of SEQ ID NO: 14;
- (viii) residues Asp29-Met215 of SEQ ID NO: 14;
- (ix) residues Asp29-Pro209 of SEQ ID NO: 14;
- (x) residues Asp29-Arg245 of SEQ ID NO: 14;
- (xi) residues Asp29-Met96 of SEQ ID NO: 14, or
- (xii) residues Trp108-Val208 of SEQ ID NO: 14.

58. (Currently Amended) The method of claim 53, wherein the administered composition comprises one or more polypeptide fragment selected from: at least one of SEQ ID NOs: 2-11.

- (a) K/QSVS/VFSYKG [SEQ ID NO: 28];
- (b) KIMIGVERTS [SEQ ID NO: 3, 10];
- (c) RIESLPIKPRG [SEQ ID NO: 5];
- (d) KH/NWS/NIWQIQDSGK [SEQ ID NO: 29];
- (e) RIGQDDLPGFDLISQFQI/VDKA [SEQ ID NO: 30];
- (f) RH/NLYPN/SGLPEEYSFLTTFR [SEQ ID NO: 31];
- (g) FSNLP/SSLFDSQWHKI [SEQ ID NO: 32]; and
- (h) RSSATLFVDCNRI [SEQ ID NO: 11].

59. (Currently Amended) The method of claim 42, wherein said administering induces A method of inducing cartilage formation in ~~an~~ the individual, comprising administering to the individual the polypeptide produced by the method of claim 29.

60. (Currently Amended) The method of claim 59, wherein the administered composition comprises one or more polypeptide fragment has having a molecular weight of:

- a) less than 30,000 Da, or
- b) less than 30,000 Da and greater than or equal to 10,000 Da.

61. (Currently Amended) The method of claim 59, wherein the administered composition comprises one or more polypeptide fragment has having an amino acid length of less than 250 amino acids.

62. (Currently Amended) The method of claim 59, wherein the ~~NC4 domain of collagen type IX alpha 1 chain comprises an amino acid sequence~~ administered composition comprises one or more polypeptide fragment having identity to SEQ ID NO: 1, SEQ ID NO: 14, SEQ ID NO: 16, or SEQ ID NO: 18 that is:

- a) at least 80~~70~~%;
- b) at least 90%; or
- c) 100%.

63. (Currently Amended) The method of claim 59, wherein the composition comprises one or more polypeptide comprises fragment selected from:

- (a) K/QSVS/V/A/EFSYKG [SEQ ID NO: 20];
- (b) KI/LMIG/SVER/TS/T [SEQ ID NO: 21];
- (c) KLGNNVDFRI [SEQ ID NO: 4];
- (d) R/KI/VES/TLP/NIKPR/KG [SEQ ID NO: 22];
- (e) KH/N/YWS/N/TIWOIQDS/AGK/R [SEQ ID NO: 23];
- (f) RIGQDDLPGFDLISQFQI/VD/EKA [SEQ ID NO: 24];
- (g) R/SH/N/AL/IYPN/SGLPE/DEYSFLTTFR [SEQ ID NO: 25];
- (h) FS/LN/HLP/SS/FLFDSQ/RWHKI/L [SEQ ID NO: 26]; and
- (i) R/TS/TSA/VTLFV/IDCN/IR/KI/V [SEQ ID NO: 27].

- (i) — residues Ile21—Gly182 of SEQ ID NO: 1;
- (ii) — residues Lys60—Arg181 of SEQ ID NO: 1;
- (iii) — residues Arg72—Arg181 of SEQ ID NO: 1;
- (iv) — residues Lys98—Gly182 of SEQ ID NO: 1;
- (v) — residues Lys123—Gly182 of SEQ ID NO: 1;
- (vi) — residues Ile24—Val208 of SEQ ID NO: 14;
- (vii) — residues Asp29—Val208 of SEQ ID NO: 14;
- (viii) — residues Asp29—Met215 of SEQ ID NO: 14;
- (ix) — residues Asp29—Pro209 of SEQ ID NO: 14;
- (x) — residues Asp29—Arg245 of SEQ ID NO: 14,

- (xi) — residues Asp29 — Met96 of SEQ ID NO: 14, or
- (xii) — residues Trp108 — Val208 of SEQ ID NO: 14.

64. (Currently Amended) The method of claim 59, wherein the composition comprises one or more polypeptide of collagen type IX alpha 1 chain comprises fragment selected from; at least one of SEQ ID NOS: 2-11.

- (a) K/QSVS/VFSYKG [SEQ ID NO: 28];
- (b) KIMIGVERTS [SEQ ID NO: peptide 3, 10];
- (c) RIESLPIKPRG [SEQ ID NO: 5];
- (d) KH/NWS/NIWQIQDSGK [SEQ ID NO: 29];
- (e) RIGQDDLPFGFDLISQFQI/VDKA [SEQ ID NO: 30];
- (f) RH/NLYPN/SGLPEEYSFLTTFR [SEQ ID NO: 31];
- (g) FSNLP/SSLFDSQWHKI [SEQ ID NO: 32]; and
- (h) RSSATLFVDCNRI [SEQ ID NO: 11].

65. (New) The composition of claim 29, wherein the composition comprises one or more polypeptide fragment selected from:

- (a) K/QSVS/VFSYKG [SEQ ID NO: 28];
- (b) KIMIGVERTS [SEQ ID NO: 3, 10];
- (c) RIESLPIKPRG [SEQ ID NO: 5];
- (d) KH/NWS/NIWQIQDSGK [SEQ ID NO: 29];
- (e) RIGQDDLPFGFDLISQFQI/VDKA [SEQ ID NO: 30];
- (f) RH/NLYPN/SGLPEEYSFLTTFR [SEQ ID NO: 31];
- (g) FSNLP/SSLFDSQWHKI [SEQ ID NO: 32]; and
- (h) RSSATLFVDCNRI [SEQ ID NO: 11].

66. (New) A method of treating or preventing in an individual an immune response to an antigenic component of collagen, comprising:

administering to the individual an isolated polypeptide or fragment thereof, the polypeptide having at least 65% identity to SEQ ID NO: 14;  
wherein said administering induces tolerance to said at least one antigenic component of collagen.